Access DB# 75762

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jennifer Maynard Examiner #: 76530 Date: 13 September 2002
Art Unit: 3763 Phone Number 305-1356 Serial Number: 09/811754
Mail Box and Bldg/Room Location: CP2-3E16 Results Format Preferred (circle): (PAPER) DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: USE of Streptomyces Hyaluroliticus Enzyme in Opthalmic Treatments

Inventors (please provide full names): Christopher Ed Schuler

Earliest Priority Filing Date: 19 March 2001

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Method comprising:

#1 injecting a solution containing hyaluronidase from Streptomyces hyaluroliticus to provide a dose of at least 10 Turbity Reducing Units (TRU) of said hyaluronidase into the vitreous humor, wherein the solution is essentially free of contaminating protease.

Method comprising:

#2 applying essentially protease-free hyaluronidase from Streptomyces hyaluroliticus to the eye.

The method is directed to clearing hemorrhagic blood from the vitreous humor of an eye; softening the cornea prior to refractive correction; spreading local anesthesia more effectively through ocular tissue prior to surgical intervention; or relating of collagen to produce contact lenses; stimulating the flow of physiological fluids in the eye so as to treat glaucoma, thrombosis, detached or impending detached retina, or for the non-surgical removal of obstructions.

13 September 2002 J Maynard

intro into body
A61M-031/00
604/521.000

** See attached COPY of CLAIMS.

****

STAFF USE ONLY

Searcher: JEANNE HORRIGAN
Searcher Phone #: 305-5934
Searcher Location: CP2-2C08
Date Searcher Picked Up: 9/27
Date Completed: 9/27
Searcher Prep & Review Time: 125
Clerical Prep Time:
Online Time: 30

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic ✓
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN ✓
Dialog ✓
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet ✓ Clinited search for true definition
Other (specify)

PTO-1590 (8-01)

12:15 3:25
9/27

File 350:Derwent WPIX 1963-2002/UD,UM &UP=200262
File 344:Chinese Patents Abs Aug 1985-2002/Sep
File 347:JAPIO Oct 1976-2002/May(Updated 020903)
File 371:French Patents 1961-2002/BOPI 200209

Set	Items	Description
S1	23	AU='SCHULER C'
S2	35	AU='SCHULER E'
S3	3662	HYALURO?
S4	0	S1:S2 AND S3

File 348:EUROPEAN PATENTS 1978-2002/Sep W03
File 349:PCT FULLTEXT 1983-2002/UB=20020912,UT=20020905
>>>No sets currently exist
[Inventor's name is not listed in these two databases.]

10/6/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
12770186 21622947 PMID: 11748958
Plasmodium falciparum cytoadherence to human placenta: evaluation of hyaluronic acid and chondroitin 4-sulfate for binding of infected erythrocytes.

16/6/3 (Item 3 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.
11459426 BIOSIS NO.: 199800240758
B-scan ultrasound examination of enzymatic vitreous liquefaction.
1998

16/6/4 (Item 4 from file: 155)
DIALOG(R)File 155:
09951822 98380468 PMID: 9712871
HYAL2, a human gene expressed in many cells, encodes a lysosomal hyaluronidase with a novel type of specificity.
Aug 28 1998

16/6/5 (Item 5 from file: 155)
DIALOG(R)File 155:
09833386 98271626 PMID: 9608699
Screening of pharmaceuticals and drugs in synovial fluid of the knee joint and in vitreous humor by fluorescence polarization immunoassay (FPIA).
May 1998

16/6/6 (Item 6 from file: 155)
DIALOG(R)File 155:
08352831 95112769 PMID: 7813399
Quantitative analysis of hyaluronan in vitreous humor using capillary electrophoresis
Jul 1994

16/6/7 (Item 7 from file: 155)
DIALOG(R)File 155:
07833989 93363676 PMID: 8357865
Optimization of the USP assay for hyaluronidase .
Apr-May 1993

16/6,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:

07191492 92104245 PMID: 1729132
Mammalian vitreous humor contains networks of hyaluronan molecules: electron microscopic analysis using the hyaluronan-binding region (G1) of aggrecan and link protein.
Feb 1992
Vitreous humor from human, bovine, and chicken eyes was analyzed by rotary shadowing to characterize further the...
...234, 1988), while G1 did not. Digestion of the chicken vitreous collagen fibrils with Streptomyces hyaluronidase did not result in the removal of the glycosaminoglycan coat of the collagen fibrils nor...
... specific binding properties can be used as probes to investigate the structure of the native vitreous humor gel from several species and suggest that this method potentially can be used for structural...

16/6,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:
05871577 88307893 PMID: 3407915
Quantitation of hyaluronic acid in tissues by ion-pair reverse-phase high-performance liquid chromatography of oligosaccharide cleavage products.
May 15 1988
... assay uses ion-pair HPLC to resolve and quantify the oligosaccharide end products of Streptomyces hyaluronidase digestion. Tissue samples were solubilized by papain, and the nondiffusate after dialysis was exhaustively digested with Streptomyces hyaluronidase . The resulting tetrasaccharide and hexasaccharide cleavage products were resolved by reverse-phase high-performance liquid...
... of other tissues including nucleus pulposus, annulus fibrosus, skin, aorta, cervix, cockscomb, synovial fluid, and vitreous humor . Results on human articular cartilage showed a linear increase in the content of hyaluronate from...

16/6,K/12 (Item 12 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.
04181212 BIOSIS NO.: 000077007256
PARAMETERS INFLUENCING OVUM PICKUP BY OVIDUCTAL FIMBRIA IN THE GOLDEN HAMSTER
1983
...ABSTRACT: they were partially tissue-specific as they would only pick up tissues such as the vitreous humor and loose connective tissue, which contain considerable extracelluar glycosaminoglycan. Interaction of cumulus and fimbria could...
...as poly-l-lysine, cationic ferritin and protamine. Treatment of fimbria with proteolytic enzymes or hyaluronidase did not prevent pickup, but neuraminidase did. The only artificial cumulus the fimbria would pick...

16/6,K/13 (Item 13 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.
02400450 BIOSIS NO.: 000065057492
THE NATURE AND ORIGIN OF THE GLYCOSAMINO GLYCANS OF THE EMBRYONIC CHICK VITREOUS BODY
1978
...ABSTRACT: vitreous were characterized and then were used as markers to establish which tissues synthesize the vitreous humor during development. The GAG are predominantly chondroitin sulfates by several criteria. They are resistant to Streptomyces hyaluronidase , an enzyme which degrades only hyaluronate and are digested by testicular hyaluronidase and chondroitinase AC, enzymes which degrade hyaluronate

plus chondroitin 4- and 6-sulfates. On electrophoresis...
...using incorporation of radioactive precursors into chondroitin sulfates in vitro, the tissues which synthesize the vitreous humor in the developing eye are determined. Late in development, on days 12-13, the isolated...
...retain similar amounts and types of GAG, indicating that cells within the vitreous synthesize the vitreous humor GAG at this time. Earlier in development, from days 6-8, the isolated vitreous incorporates...
...following incorporation, the vitreous retains more radioactive chondroitin sulfate than does the neural retina. The vitreous humor GAG is initially synthesized by the neural retina and is secreted into the vitreous space.
DESCRIPTORS: STREPTOMYCES HYALURONIDASE RETINA CHONDROITIN 4 SULFATE CHONDROITIN 6 SULFATE ELECTROPHORESIS

16/6/15 (Item 15 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.
01622895 BIOSIS NO.: 000059022904
VISCOSITY MEASUREMENTS OF BOVINE VITREOUS HUMOR FOR INVESTIGATION OF MOLECULAR CHANGES OF HYALURONIC-ACID BY ASCORBIC-ACID
1974

16/6/16 (Item 16 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.
09812886 BIOSIS NO.: 199598267804
Human vitreous inhibits interferon-alpha production by alloantigen-activated peripheral blood lymphocytes.

16/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.
12673315 BIOSIS NO.: 200000426817
Method for accelerating clearance of hemorrhagic blood from the vitreous body with hyaluronidase .
AUTHOR: Karageozian Hampar L(a); Karageozian Vicken H; Kenney Maria Cristina; Gutierrez Flores Jose Luis; Carpio Aragon Gabriel Arturo; Nesburn Anthony B
AUTHOR ADDRESS: (a)San Juan Capistrano, CA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1232 (3):pNo pagination Mar. 21, 2000
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: A thimerosal-free hyaluronidase is prepared wherein the preferred hyaluronidase is devoid of molecular weight fractions below 40,000 MW, between 60-70,000 MW and above 100,000 MW. Also a method for accelerating the clearance of hemorrhagic blood from the vitreous humor of the eye is carried out by contacting at least one hemorrhage-clearing enzyme (e.g., hyaluronidase , beta-glucuronidase, matrix metalloproteinase, chondroitinase, chondroitin sulfatase or protein kinase) with the vitreous humor in an amount which is effective to cause accelerated clearance of blood therefrom.

16/7/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

11864896 BIOSIS NO.: 199900111005
Method for accelerating clearance of hemorrhagic blood from the vitreous humor with hyaluronidase .
AUTHOR: Harageozian H L; Karageozian V H; Capistrano J; Kenney M C; Flores J L G; Aragon G A C; Nesburn A B
AUTHOR ADDRESS: San Juan Capistrano, Calif.**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1219 (1):p429 Feb. 2, 1999
ISSN: 0098-1133
RECORD TYPE: Citation
LANGUAGE: English

16/7/10 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

03730739 EMBASE No: 1988180175
Viscosity of subretinal fluid - Relationship with composition and clinical findings
Matsuda K.
Department of Ophthalmology, Yamaguchi University, School of Medicine, Yamaguchi Japan
Journal of Japanese Ophthalmological Society (J. JPN. OPHTHALMOL. SOC.) (Japan) 1988, 92/4 (611-618)
CODEN: NGZAA ISSN: 0029-0203
DOCUMENT TYPE: Journal
LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH
The viscosity of subretinal fluid was measured with a cone-plate viscometer. Subretinal fluid exhibited non-Newtonian behavior, showing pseudoplastic viscosity, i.e. the viscosity was higher at low shear rates. The distribution of viscosity of subretinal fluids was higher than in serum and equal to or higher than that of liquefied vitreous fluid. Subretinal fluid and liquefied vitreous fluid are pseudoplastic fluids in contrast to serum which is a Newtonian fluid, i.e. viscosity is the same at all shear rates. There was a significant correlation between the viscosity and hyaluronate contents of subretinal fluid. On the other hand, there was no correlation between the viscosity and protein and glycopeptide contents. Hyaluronidase treatment decreased the viscosity of subretinal fluid. These results revealed that hyaluronate caused viscosity in subretinal fluid as well as vitreous humor . The relationship between the clinical findings of various kinds of retinal detachments and the viscosity of subretinal fluid was evaluated by students t-test and multivariate analysis containing quantification I and multiple regression using the computerized statistics program package SPSS. There was a tendency for aphakia or total detachment to correlate with lower subretinal fluid viscosity.

File 155:MEDLINE(R) 1966-2002/Sep W4
File 144:Pascal 1973-2002/Sep W4
File 5:Biosis Previews(R) 1969-2002/Sep W4
File 6:NTIS 1964-2002/Sep W5
File 8:Ei Compendex(R) 1970-2002/Sep W3
File 99:Wilson Appl. Sci & Tech Abs 1983-2002/Aug
File 238:Abs. in New Tech & Eng. 1981-2002/Sep
File 65:Inside Conferences 1993-2002/Sep W4
File 77:Conference Papers Index 1973-2002/Sep

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File  73:EMBASE 1974-2002/Sep W4
File  34:SciSearch(R) Cited Ref Sci 1990-2002/Sep W5
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
File  94:JICST-EPlus 1985-2002/Jul W4
File  35:Dissertation Abs Online 1861-2002/Aug
Set     Items   Description
S1          0   E2
S2       3887   VITREOUS()(HUMOR OR HUMOUR)
S3      17382   HYALURONIDASE
S4         53   STREPTOMYCES()HYALUROLYTICUS
S5     247583   PROTEASE
S6       4096   TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7         39   S2 AND S3
S8          0   S6 AND S7
S9          5   S4 AND S7
S10         1   RD (unique items)
S11         0   S7 AND S5
S12        34   S7 NOT S9
S13         1   S12/2002
S14        33   S12 NOT S13
S15        16   RD (unique items)
S16        16   Sort S15/ALL/PY,D
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11/6,K/3     (Item 3 from file: 149)
DIALOG(R)File 149:(c) 2002 The Gale Group. All rts. reserv.
01423859     SUPPLIER NUMBER: 14197940    (USE FORMAT 7 OR 9 FOR FULL TEXT)
The etiology of rheumatic fever: a review of theories and evidence.
  (Classics in Medicine)
1993
WORD COUNT:   4020    LINE COUNT:  00396
...     lately on hyaluronic acid and the various enzymes that act on it,
known collectively as  hyaluronidase . Hyaluronic acid is a
mucopolysaccharide which has been isolated from skin, synovial fluid,
mesenchymal tumors,  vitreous  humor  and umbilical cord, and which is
suspected of being an important constituent of the amorphous...
...which hyaluronic acid has actually been isolated, namely the skin,
umbilical cord, synovial fluid, and  vitreous  humor , only the skin is
involved in the rheumatic process. The hyaluronic acid in synovial fluid...

11/6,K/5     (Item 5 from file: 442)
DIALOG(R)File 442:(c)2002 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00045739
Pseudo-Schnabel's  Cavernous  Degeneration  of the Optic Nerve Secondary to
Intraocular Silicone Oil  (CLINICOPATHOLOGIC REPORTS)
 1989;
  LINE COUNT: 00142         WORD COUNT: 01973
... nerve,  which  developed  consequent  to  severe  acute  glaucoma.  The
resultant  cystic  spaces  were  filled with  hyaluronidase -sensitive acid
mucopolysaccharide,  probably of  vitreous  humor  origin. In our case the
cystic spaces were filled with silicone oil, not vitreous hyaluronic...

11/3,AB,K/1     (Item 1 from file: 16)
DIALOG(R)File  16:Gale Group PROMT(R)
(c) 2002 The Gale Group. All rts. reserv.
07731869    Supplier Number: 64506559
```

ISTA RAISES $31.5M AS WAVE OF BIOTECH IPOS SUBSIDES.
Strickland, Debbie
BIOWORLD Today, v11, n163, pNA
August 23, 2000
Language: English Record Type: Fulltext
Document Type: Magazine/Journal; Trade
Word Count: 676
... Advanced Corneal Systems, has reached the Phase III stage of clinical testing with **Vitrase, a hyaluronidase -based product for severe vitreous hemorrhage**. According to the company, the 1 million cases of...
...in its IPO filing, could probably be treated with **Vitrase, which is injected into the vitreous humor** , causing the substance to liquefy and promoting clearance of the hemorrhage...

11/3,AB,K/4 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2002 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00086876 COPYRIGHT American Medical Association 1992
Pharmacologic Induction of Posterior Vitreous Detachment in the Rabbit
VERSTRAETEN, THIERRY C.; CHAPMAN, CHRIS; HARTZER, MICHAEL; WINKLER, BARRY S.; TRESE, MICHAEL T.; WILLIAMS, GEORGE A.
Archives of Ophthalmology
June, 1993; p849
LINE COUNT: 00314
Objective.--To assay the proteolytic activity of plasmin on the vitreoretinal junction and to assess a potential facilitating effect on posterior vitreous detachment. Methods.--We injected 1 U of plasmin into the vitreous of rabbits. Some eyes underwent vitrectomy after plasmin injection. Electroretinography and electron microscopy were performed. Results.--In plasmin-treated eyes, electroretinography displayed a transient (3 days) decreased b-wave amplitude. Histologic examination demonstrated posterior vitreous detachment in eyes that received intravitreal plasmin followed by vitrectomy. Conclusion.--Plasmin may prove to be a useful biochemical adjunct to mechanical vitrectomy.
...on rabbit vitreous. Am J Ophthalmol. 1958;46:356-358.
7. Pirie A. Effect of hyaluronidase injection on vitreous humor of rabbit. Br J Ophthalmol. 1949;33:678-684...

11/3,AB,K/6 (Item 6 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2002 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00034074 Copyright (C) 1986 American Medical Association
Early Vitreous Changes in Experimental Proliferative Vitreoretinopathy (LABORATORY SCIENCES)
MIGLIOR, STEFANO; KAIN, HERMANN L.; LIBONDI, TEODOSIO; GONZALEZ, R. GILBERTO; BARNETT, PATRICK; KRAUSS, JOEL M.; CHENG, HONG-MING
Archives of Ophthalmology
November, 1986; 104: 1681-16841986;
LINE COUNT: 00204 WORD COUNT: 02828
ABSTRACT: Proton magnetic resonance imaging (MRI) was employed to obtain information on early vitreal changes preceding ophthalmoscopically visible proliferative vitreoretinopathy. **Rabbits were injected close to the posterior pole with a suspension of 250 000 cultured homologous fibroblasts**. The MRI was carried out using a 1.4-tesla (T) superconducting imager (at a proton frequency of 61.4 MHz). The images were obtained over a span of six days, prior to any detection of proliferative vitreoretinopathy

with ophthalmoscopy. **As early as two days after injection, an area of increased spin-spin relaxation time (T2) corresponding to the vitreal injection site became visible.** The MRI observations paralleled in vitro changes in proton relaxation times (T1 (Ref. spi-latticerelaxatiotime) and T2) after addition of beta-N-acetylglucosaminidase to the vitreous. Our **data suggest that hyaluronate disruption due to the activity of fibroblastic enzymes may result in fibroblast dispersion and movement in the vitreous and that MRI can provide early signs of vitreal changes that lead to retinal detachment.**

CITED REFERENCES:

... Algvere P, Kock E: Experimental fibroplasia in the rabbit vitreous: Effects of hyaluronidase and implantation of autologous dermal tissue. Graefes Arch Clin Exp Ophthalmol 1976;199:133-139...

...Cell. New York, Garland Publishing Inc, 1983, pp 702-703.

26. Reeser FH, Aaberg TM: Vitreous humor , in Duane TD, Jaeger EA (eds): Biomedical Foundations of Ophthalmology. New York, Harper & Row Publishers...

11/3,AB,K/7 (Item 7 from file: 442)
DIALOG(R)File 442:AMA Journals

Hyaluronidase and Retinal Function (LABORATORY SCIENCES)

WINKLER, BARRY S.

Archives of Ophthalmology
November, 1985; 103: 1743-17461985;
LINE COUNT: 00222 WORD COUNT: 03065

ABSTRACT: Using the incubated isolated rat retina, the effects of hyaluronidase on the electroretinogram (ERG) and metabolic activities were investigated. Initial experiments established the activity of hyaluronidase needed to liquefy, within 15 to 30 minutes, the vitreous of postmortem human eyes; this concentration was 1,000 units/mL. Rat retinas were superfused with a bicarbonate-buffered, oxygenated medium to which hyaluronidase was added in activities ranging from 100 to 5,000 units/mL. These concentrations of hyaluronidase did not significantly alter the amplitudes of the a waves and b waves of the ERG in comparison to their control amplitudes. Measurements were also made of lactic acid production, oxygen consumption, glutathione content, and adenosine triphosphatase activities in control and hyaluronidase-exposed retinas. In the presence of hyaluronidase, their respective values were similar to the controls for all biochemical factors studied. **The present experiments demonstrate that addition of hyaluronidase to an "ocular irrigating" solution results in normal ERGs and normal retinal metabolic activity and suggests the possibility that hyaluronidase may be useful in enzyme-assisted vitrectomy.** ... **The objective of the present study was to determine the in vitro effects of hyaluronidase on the ERG potentials and metabolic activities of the superfused isolated rat retina.** The results demonstrate that addition of hyaluronidase to the incubation medium, at concentrations that liquefy the vitreous humor , results in normal ERGs and normal metabolic activities.

METHODS

Adult albino rats weighing between 175...retinal preparations over long periods of time.

Hyaluronic acid is a major component of the vitreous humor and contributes to its gellike state. Hyaluronidase is an enzyme that degrades hyaluronic acid as well as chondroitin and chondroitin sulfates;

this...
... possibility whether digestion of the vitreous could be a useful adjunct to vitrectomy, and whether hyaluronidase could be safely used in this clinical procedure. The present study has attempted to establish the toxic effects of hyaluronidase on retinal function.
Adding hyaluronidase to the incubation medium in concentrations that appear to liquefy...

11/7/2 (Item 2 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)

06712630 Supplier Number: 56194979 (THIS IS THE FULLTEXT)
Advanced Corneal Systems obtains United States patent.
BIOTECH Patent News, v13, n9, pNA
Sept, 1999
TEXT:
Advanced Corneal Systems, Inc. (Irvine, CA) has patented a thimerosal-free hyaluronidase preparation wherein the preferred hyaluronidase enzyme is devoid of molecular weight fractions below 40,000 MW, between 60-70,000 MW and above 100,000 MW. Also disclosed is a method for accelerating the clearance of hemorrhagic blood from the vitreous humor of the eye, comprising the step of contacting at least one hemorrhage-clearing enzyme (e.g., a Beta -glucuronidase, matrix metalloproteinase, chondroitinase, chondroitin sulfatase or protein kinase) with the vitreous humor in an amount which is effective to cause accelerated clearance of blood therefrom. (US 5866120)

File 95:TEME-Technology & Management 1989-2002/Sep W4
File 98:General Sci Abs/Full-Text 1984-2002/Aug
File 9:Business & Industry(R) Jul/1994-2002/Sep 26
File 16:Gale Group PROMT(R) 1990-2002/Sep 27
File 160:Gale Group PROMT(R) 1972-1989
File 148:Gale Group Trade & Industry DB 1976-2002/Sep 27
File 621:Gale Group New Prod.Annou.(R) 1985-2002/Sep 26
File 636:Gale Group Newsletter DB(TM) 1987-2002/Sep 27
File 441:ESPICOM Pharm&Med DEVICE NEWS 2002/Sep W4
File 20:Dialog Global Reporter 1997-2002/Sep 27
File 813:PR Newswire 1987-1999/Apr 30
File 15:ABI/Inform(R) 1971-2002/Sep 27
File 88:Gale Group Business A.R.T.S. 1976-2002/Sep 26
File 442:AMA Journals 1982-2002/Sep B2
File 444:New England Journal of Med. 1985-2002/Sep W5
File 149:TGG Health&Wellness DB(SM) 1976-2002/Sep W3

Set	Items	Description
S1	0	E2
S2	532	VITREOUS()(HUMOR OR HUMOUR)
S3	922	HYALURONIDASE
S4	1	STREPTOMYCES()HYALUROLYTICUS
S5	32802	PROTEASE
S6	10463	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	11	S2(S)S3
S8	9	RD (unique items)
S9	2	S8/2002
S10	7	S8 NOT S9

S11 7 Sort S10/ALL/PD,D

8/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012588864 **Image available**
WPI Acc No: 1999-394971/199933
Purification and sequencing of hyaluronidase isoenzymes
Patent Assignee: UNIV CALIFORNIA (REGC)
Inventor: CSOKA A; FROST G I; STERN R; WONG T M
Number of Countries: 084 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9929841	A1	19990617	WO 98US24206	A	19981112	199933	B
AU 9915855	A	19990628	AU 9915855	A	19981112	199946	
EP 1036168	A1	20000920	EP 98960197	A	19981112	200047	
			WO 98US24206	A	19981112		
US 6123938	A	20000926	US 96733360	A	19961017	200051	
			US 97987743	A	19971209		
JP 2001526183	W	20011218	WO 98US24206	A	19981112	200203	
			JP 2000524414	A	19981112		

Priority Applications (No Type Date): US 97987743 A 19971209; US 96733360 A 19961017
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9929841	A1	E	62	C12N-015/11	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9915855	A		C12N-015/11	Based on patent WO 9929841
EP 1036168	A1	E	C12N-015/11	Based on patent WO 9929841

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 6123938	A		A61K-038/46	CIP of application US 96733360
JP 2001526183	W	68	C07K-014/00	Based on patent WO 9929841

Abstract (Basic): WO 9929841 A1

NOVELTY - A method for purification and sequencing of isoenzymes of plasma hyaluronidase (pHAse) found in the urine, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated human urinary hyaluronidase (huHAse);

(2) isolated chain A and B polypeptides of huHAse;

(3) polynucleotide sequences encoding the huHAse A or B chain;

(4) a polynucleotide sequence probe comprising at least 15 contiguous nucleotides of the polynucleotide sequence of (3);

(5) a recombinant expression vector comprising polynucleotides encoding huHAse A or B chains;

(6) an isolated recombinant host cell containing the expression vector of (5);

(7) a purified antibody that specifically binds a huHAse or huHAse A or B chain; and

(8) purification of huHAse from a sample comprises contacting the

sample with anti-huHAse antibody and detecting for the formation of anti-huHAse antibody-huHAse complexes.

ACTIVITY - Cytostatic; Ophthalmological.

MECHANISM OF ACTION - None given.

USE - Hyaluronidase is useful as a therapeutic in the treatment of diseases associated with excess hyaluronan and to enhance circulation of physiological fluids and/or therapeutic agents at the site of administration. **Hyaluronidase can be used to reduce intraocular pressure in the eyes of glaucoma patients, through degradation of hyaluronan within the vitreous humor.** It can also be used in cancer therapy as a spreading agent to enhance the activity of chemotherapeutics and/or the accessibility of tumors to chemotherapeutics. In particular, the hyaluronidase is useful in cancer therapy for cancers associated with a defect in the tumor suppressor gene LuCa-1 and also in treatment of strokes or myocardial infarction. It can also be used to facilitate clysis, particularly hypodermoclysis and also for treatment of certain lysosomal storage diseases associated with defects in hyaluronidase . A lysosomal storage disease amenable to huHAse therapy are those resulting in accumulation of (GlcNAcbeta1-4GlcUAbeta1-3)n (GAGs) due to a defective mannose-6-phosphate pathway.

ADVANTAGE - The purified human urinary hyaluronidase is more appropriate for therapeutic uses than the presently available commercial formulations of hyaluronidase (e.g. WYDASE, a bovine hyaluronidase formulation) which are from a non-human source, which contain two hyaluronidases (rather than one), and which, as determined by SDS-PAGE analysis, are very crude mixtures containing various proteins, including several unidentified proteins and proteins having various biological activities including anticoagulant activities. The current purified huHAse provides a clean source of hyaluronidase that is less likely to induce some of the side effects associated with the presently available commercial formulation, and allows better control of the level of activity associated with specific dosages.

Additionally, use of an acid active huHAse is preferred to use of neutral hyaluronidase (HAses) since acid active HAses can yield a controlled degradation of a HA substrate and does not degrade all components of the extracellular matrix in the patient. The huHAse also has a lower molecular weight, allowing the enzyme to enter cells more readily than other, higher molecular weight HAses.

DESCRIPTION OF DRAWING(S) - pH activity curve or human urinary hyaluronidase using a microtiter assay.

pp; 62 DwgNo 4/4

Derwent Class: B04; D16
International Patent Class (Main): A61K-038/46; C07K-014/00; C12N-015/11
International Patent Class (Additional): A01N-037/18; A61K-038/00; A61K-038/54; A61P-009/10; A61P-027/06; A61P-035/00; C07K-001/00; C07K-016/40; C12N-001/15; C12N-001/19; C12N-001/21; C12N-005/10; C12N-009/42; C12N-015/09; C12Q-001/68; C12R-001-93

9/26,TI/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX

007020994
WPI Acc No: 1987-020991/198703
Determn. of hyaluronidase activity by incubation - involves using vitreous humour of eye as substrate for hydrolysis evaluation to simplify method

9/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012264024
WPI Acc No: 1999-070130/199906
Method for inducing liquefaction of vitreous humor to prevent eye disorder in mammal - comprises contacting vitreous humor with hyaluronidase to liquefy vitreous humor without causing toxic damage to eye
Patent Assignee: ISTA PHARM INC (ISTA-N); ADVANCED CORNEAL SYSTEMS INC (ADCO-N)
Inventor: ARAGON G A C; FLORES J L G; KARAGEOZIAN H L; KARAGEOZIAN V H; KENNEY M C; NESBURN A B
Number of Countries: 083 Number of Patents: 009
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9852602	A1	19981126	WO 98US10578	A	19980522	199906	B
AU 9876936	A	19981211	AU 9876936	A	19980522	199917	
EP 983084	A1	20000308	EP 98924866	A	19980522	200017	
			WO 98US10578	A	19980522		
BR 9809558	A	20000704	BR 989558	A	19980522	200040	
			WO 98US10578	A	19980522		
CN 1257430	A	20000621	CN 98805342	A	19980522	200049	
MX 9910495	A1	20000501	MX 9910495	A	19991115	200129	
KR 2001012787	A	20010226	KR 99710750	A	19991120	200154	
JP 2002503229	W	20020129	JP 98550719	A	19980522	200211	
			WO 98US10578	A	19980522		
AU 200193449	A	20020117	AU 9876936	A	19980522	200219	N
			AU 200193449	A	20011127		

Priority Applications (No Type Date): US 97862620 A 19970522; AU 200193449 A 20011127
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9852602	A1	E	44	A61K-038/47	
	Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW				
	Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW				
AU 9876936	A			A61K-038/47	Based on patent WO 9852602
EP 983084	A1	E		A61K-038/47	Based on patent WO 9852602
	Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE				
BR 9809558	A			A61K-038/47	Based on patent WO 9852602
CN 1257430	A			A61K-038/47	
MX 9910495	A1			A61K-038/47	
KR 2001012787	A			A61K-038/47	
JP 2002503229	W		59	A61K-038/46	Based on patent WO 9852602
AU 200193449	A			A61K-038/47	Div ex application AU 9876936

Abstract (Basic): WO 9852602 A

A method for inducing liquefaction of a vitreous humor to prevent a disorder of a mammalian eye comprises contacting the vitreous humor with hyaluronidase, without causing toxic damage to the eye.

The method is used to treat proliferative retinopathy, age-related macular degeneration, amblyopia, retinitis pigmentosa, macular holes, macular exudates and cystoid macular oedema. Hyaluronidase is administered at 5-200

(especially 1) IU in multiple doses as intra-vitreal injections (injection volume < 200 mu l). The method is applied when the vitreous humor is free of haemorrhagic blood so that the retina can be viewed (all claimed).
Dwg.0/6
Derwent Class: B04; D16
International Patent Class (Main): A61K-038/46; A61K-038/47
International Patent Class (Additional): A61K-009/08; A61P-003/10; A61P-027/02

9/7/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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011319972
WPI Acc No: 1997-297876/199727
Clearing haemorrhagic blood from the vitreous humor by injecting enzyme - specifically new non-toxic, thiomerosal-free hyaluronidase formulation, to make possible ophthalmic examination of injured retinas
Patent Assignee: ISTA PHARM INC (ISTA-N); ADVANCED CORNEAL SYSTEMS INC (ADCO-N); ARAGON C (ARAG-I); GUTIERREZ FLORES J L (FLOR-I); KARAGEOZIAN H L (KARA-I); KARAGEOZIAN V H (KARA-I); KENNEY M C (KENN-I); NESBURN A B (NESB-I); ADVANCED CORNEAL SYSTEMS (ADCO-N)
Inventor: ARAGON G A C; FLORES J L G; KARAGEOZIAN H L; KARAGEOZIAN V H; KENNEY M C; NESBURN A B; ARAGON G A; ARAGON C; GUTIERREZ FLORES J L; CARPIO ARAGON G A
Number of Countries: 072 Number of Patents: 012
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9718835	A1	19970529	WO 96US18843	A	19961120	199727	B
AU 9714070	A	19970611	AU 9714070	A	19961120	199740	
EP 862456	A1	19980909	EP 96944203	A	19961120	199840	
			WO 96US18843	A	19961120		
US 5866120	A	19990202	US 95561636	A	19951122	199912	
BR 9611617	A	19990406	BR 9611617	A	19961120	199920	
			WO 96US18843	A	19961120		
CN 1207684	A	19990210	CN 96199746	A	19961120	199925	
US 6039943	A	20000321	US 95561636	A	19951122	200021	
			US 98139282	A	19980824		
JP 2000502325	W	20000229	WO 96US18843	A	19961120	200022	
			JP 97519951	A	19961120		
MX 9804051	A1	19981201	MX 984051	A	19980521	200024	
KR 99071565	A	19990927	WO 96US18843	A	19961120	200048	
			KR 98703840	A	19980522		
AU 200053402	A	20001026	AU 9714070	A	19961120	200059	N
			AU 200053402	A	20000816		
US 20020071837	A1	20020613	US 95561636	A	19951122	200243	
			US 98139282	A	19980824		
			US 99453012	A	19991202		

Priority Applications (No Type Date): US 95561636 A 19951122; US 98139282 A 19980824; AU 200053402 A 20000816; US 99453012 A 19991202
Cited Patents: 6.Jnl.Ref; US 4174389; US 5260059; US 5292509
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9718835	A1	E	44	A61K-038/43	

Designated States (National): AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GR IE IT KE

LS LU MC MW NL OA PT SD SE SZ UG
AU 9714070 A A61K-038/43 Based on patent WO 9718835
EP 862456 A1 E A61K-038/43 Based on patent WO 9718835
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5866120 A A61K-038/43
BR 9611617 A A61K-038/43 Based on patent WO 9718835
CN 1207684 A A61K-038/43
US 6039943 A A61K-038/43 Cont of application US 95561636
Cont of patent US 5866120
JP 2000502325 W 34 A61K-038/46 Based on patent WO 9718835
MX 9804051 A1 A61K-038/43
KR 99071565 A A61K-038/43 Based on patent WO 9718835
AU 200053402 A A61K-038/43 Div ex application AU 9714070
US 20020071837 A1 A61K-038/47 Cont of application US 95561636
Cont of application US 98139282

Abstract (Basic): WO 9718835 A

Clearance of haemorrhagic blood from the vitreous humor of a mammal comprise treating the humour with an enzyme (I).

Also claimed is a hyaluronidase (Ia) composition for ophthalmic administration that is free of thiomerosal (II) and of (Ia) with molecular weight (m. wt.) < 40 kDa.

USE - The treatment is used to clear intra-vitreal blood in cases of e.g. diabetic retinopathy or injury that causes rupture of, or leakage from, retinal blood vessels. Clearance is needed to allow proper trans-vitreal examination of the retina for diagnosing tears or detachment; to restore vision and to facilitate surgical procedures, without the need for vitrectomy.

(Ia) is administered by a single intra-vitreal injection at a dose of 10-300 IU, in a volume < 50 mu l, particularly in absence of (II) (claimed).

Also contemplated is a topical application.

ADVANTAGE - The new (II)-free (Ia) composition is effective without being toxic to the eye (contrast some known (Ia) formulations).

Dwg.0/6

Derwent Class: B04; D16
International Patent Class (Main): A61K-038/43; A61K-038/46; A61K-038/47
International Patent Class (Additional): A61K-009/08; A61K-031/715; A61K-038/00; A61K-038/48; A61K-047/02; A61K-047/26; A61P-027/02; C12N-009/26

9/7/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

009896351
WPI Acc No: 1994-176267/199421
Microbiological prodn. of non-antigenic hyaluronic acid for preparations replacing vitreous humor of eye - comprises growing Streptococcus equiv. in aq., chemically defined medium free of protein
Patent Assignee: MILES INC (MILE)
Inventor: BROWN K K; BRYANT S A; GREENE N D; RUIZ L L C; TRUMP S L; VAN DE RIJN I; WILSON C D
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5316926	A	19940531	US 83555224	A	19831125	199421	B
			US 85801973	A	19851126		

US 86873245 A 19860611
US 86910246 A 19860918
US 91796178 A 19911122

Priority Applications (No Type Date): US 91796178 A 19911122; US 83555224 A 19831125; US 85801973 A 19851126; US 86873245 A 19860611; US 86910246 A 19860918

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5316926	A		19	C12P-019/04	Div ex application US 83555224 Cont of application US 85801973 CIP of application US 86873245 CIP of application US 86910246 CIP of patent US 4782046

Abstract (Basic): US 5316926 A

Producing high mol.wt. hyaluronic acid (I) comprises: (a) growing a microorganism having the identifying characteristics of the strain of Streptococcus equi ATCC No. 39506 in an aq. chemically defined medium which is free of protein not released by the microorganism; (b) inactivating any extracellular hyaluronidase (II) generated by the microorganism; (c) maintaining the microorganism to essentially log phase-growth for above 24 hrs. by (i) maintaining the pH in the range 7 - 7.2 by continuous or intermittent addition of base; (ii) maintaining the temp. in the range of 37 deg.C; and (iii) adjusting the glucose content of the medium to at least 1 wt.% at least every 24 hrs., (d) isolating the generated (I) from the culture without disrupting the streptococcal cells; and (e) purifying the isolated (I) without causing any significant mol.wt. degration.

USE - Using the process suitable microorganisms can be cultured to give high yield of high mol.wt. antigen-free (I). The organisms are grown in a chemically defined medium free of protein. They are kept in log phase by appropriate pH control and addn. of dextrose (glucose) for an extended period and (I) is isolated without killing the microorganisms.

Dwg.0/10

Derwent Class: B04; D16
International Patent Class (Main): C12P-019/04
International Patent Class (Additional): C12N-001/20; C12N-015/01

File 350:Derwent WPIX 1963-2002/UD,UM &UP=200262
File 344:Chinese Patents Abs Aug 1985-2002/Sep
File 347:JAPIO Oct 1976-2002/May(Updated 020903)
File 371:French Patents 1961-2002/BOPI 200209

Set	Items	Description
S1	0	E2
S2	114	VITREOUS()(HUMOR OR HUMOUR)
S3	607	HYALURONIDASE
S4	5	STREPTOMYCES()HYALUROLYTICUS
S5	14661	PROTEASE
S6	180	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	5	S2 AND S3
S8	**1**	**S7 AND S4:S6**
S9	**4**	**S7 NOT S8**

9/6/2 (Item 1 from file: 349)
00498489
PURIFICATION AND MICROSEQUENCING OF HYALURONIDASE ISOZYMES

Publication Year: 1999

9/6/4 (Item 3 from file: 349)
00426192
HUMAN PLASMA HYALURONIDASE
Publication Year: 1998

9/6/6 (Item 5 from file: 349)
00349083
BH55 HYALURONIDASE
Publication Year: 1996

9/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00216435
Hyaluronidase, isolation and pharmaceutical use thereof, and pharmaceutical and veterinary formulations containing it.
Isolierung und pharmazeutische Verwendung von Hyaluronidase und diese enthaltende pharmazeutische und tierarztliche Praparate.
Isolation et utilisation pharmaceutique de l'hyaluronidase et preparations pharmaceutiques et veterinaires la contenant.
PATENT ASSIGNEE:
Merck Patent GmbH, (205222), Frankfurter Strasse 250, W-6100 Darmstadt, (DE), (applicant designated states: DE;FR;GB;IT)
INVENTOR:
Sawyer, Roy Thomas, 63 Westport Ave Mayals, Swansea West Glamorgan SA3 5EF, (GB)
Edwards, Jeffrey, 18 Pentre Road Pontardulais, Swansea West Glamorgan SA4 1HT, (GB)
LEGAL REPRESENTATIVE:
Austin, Hedley William et al (45852), Urquhart-Dykes & Lord Alexandra House 1 Alexandra Road, Swansea West Glamorgan SA1 5ED, (GB)
PATENT (CC, No, Kind, Date): EP 193330 A2 860903 (Basic)
EP 193330 A3 880720
EP 193330 B1 930721
APPLICATION (CC, No, Date): EP 86301092 860217;
PRIORITY (CC, No, Date): GB 8504025 850216
DESIGNATED STATES: DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: C12N-009/26; A61K-037/54; C12Q-001/34
ABSTRACT EP 193330 A2
Hyaluronidase, isolation and pharmaceutical use thereof, and pharmaceutical and veterinary formulations containing it.

The hyaluronidase, which is a hyaluronic acid-specific endo-b-glucuronidase, having a molecular weight of about 28,500 in non-reduced form, is derived from buffalo leeches (that is, leeches of the sub-family Hirudinariinae, such as the species Hirudinaria manillensis or Poecilobdella granulosa)

The hyaluronidase, which cleaves hyaluronic acid, but not chondroitin, chondroitin -4- sulphate, chondroitin -6- sulphate or heparin, is considerably more stable at high temperatures and extremes of pH than known leech hyaluronidase. It has a wide range of uses where breakdown of hyaluronic acid is required; of particular interest is in pharmaceutical or veterinary formulations, either as an active agent or a spreading or percutaneous factor. **The hyaluronidase is useful for stimulating flow of physiological fluids in the eye (for example, in the treatment of glaucoma).**
ABSTRACT WORD COUNT: 140

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	273
CLAIMS B	(German)	EPBBF1	244
CLAIMS B	(French)	EPBBF1	278
SPEC B	(English)	EPBBF1	3480
Total word count - document A			0
Total word count - document B			4275
Total word count - documents A + B			4275

9/3,AB/3 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00462138
USE OF HYALURONIDASE IN THE MANUFACTURE OF AN OPHTHALMIC PREPARATION FOR LIQUEFYING VITREOUS HUMOR IN THE TREATMENT OF EYE DISORDERS
UTILISATION DE L'HYALURONIDASE DANS LA FABRICATION D'UNE PREPARATION OPHTALMIQUE DESTINEE A FLUIDIFIER L'HUMEUR VITREUSE DANS LE TRAITEMENT DE CERTAINS TROUBLES OCULAIRES
Patent Applicant/Assignee:
ADVANCED CORNEAL SYSTEMS INC,
KARAGEOZIAN Hampar L,
KARAGEOZIAN Vicken H,
KENNEY Maria Cristina,
FLORES Jose Luis Gutierrez,
ARAGON Gabriel Arturo Carpio,
NESBURN Anthony B,
Inventor(s):
KARAGEOZIAN Hampar L,
KARAGEOZIAN Vicken H,
KENNEY Maria Cristina,
FLORES Jose Luis Gutierrez,
ARAGON Gabriel Arturo Carpio,
NESBURN Anthony B,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9852602 A1 19981126
Application: WO 98US10578 19980522 (PCT/WO US9810578)
Priority Application: US 97862620 19970522
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 14241
English Abstract
An enzymatic method is provided for treating ophthalmic disorders of the mammalian eye. Prevention of neovascularization and the increased rate of clearance from the vitreous of materials toxic to retina is accomplished by administering an amount of hyaluronidase effective to liquefy the vitreous humor of the treated eye without causing toxic damage to the eye. Liquefaction of the vitreous humor increases the rate of liquid exchange from the vitreal chamber. This increase in exchange removes those materials and conditions whose presence causes ophthalmological and retinal damage.

9/3,AB/5 (Item 4 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00378092
ENZYMATIC METHOD AND COMPOSITIONS FOR TREATING INTRAVITREAL HEMORRHAGIC BLOOD
PROCEDE ENZYMATIQUE ET COMPOSITIONS POUR LE TRAITEMENT DE SANG D'HEMORRAGIE INTRAVITREENNE
Patent Applicant/Assignee:
ADVANCED CORNEAL SYSTEMS INC,
Inventor(s):
KARAGEOZIAN Hampar L,
KARAGEOZIAN Vicken H,
KENNEY Maria C,
FLORES Jose L G,
ARAGON Gabriel A C,
NESBURN Anthony B,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9718835 A1 19970529
Application: WO 96US18843 19961120 (PCT/WO US9618843)
Priority Application: US 95561636 19951122
Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 6274
English Abstract
A thimerosal-free hyaluronidase preparation wherein the preferred hyaluronidase enzyme is devoid of molecular weight fractions below 40,000 MW, between 60-70,000 MW and above 100,000 MW. Also disclosed is a method for accelerating the clearance of hemorrhagic blood from the vitreous humor of the eye, said method comprising the step of contacting at least one hemorrhage-clearing enzyme (e.g., a 'beta'-glucuronidase, matrix metalloproteinase, chondroitinase, chondroitin sulfatase or protein kinase) with the vitreous humor in an amount which is effective to cause accelerated clearance of blood therefrom.

10/6/3 (Item 2 from file: 349)
00774919
HYALURONIC ACID ANTI-ADHESION BARRIER
Publication Year: 2001

10/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01013253
USE OF HYALURONIDASE IN THE MANUFACTURE OF AN OPHTHALMIC PREPARATION FOR LIQUEFYING VITREOUS HUMOR IN THE TREATMENT OF EYE DISORDERS
VERWENDUNG VON HYALURONIDASE ZUR HERSTELLUNG EINES AUGENPRAPARATS ZUR GLASSKORPERVERFLUSSIGUNG BEI DER BEHANDLUNG VON AUGENERKRANKUNGEN
UTILISATION DE L'HYALURONIDASE DANS LA FABRICATION D'UNE PREPARATION OPHTALMIQUE DESTINEE A FLUIDIFIER L'HUMEUR VITREUSE DANS LE TRAITEMENT DE CERTAINS TROUBLES OCULAIRES
PATENT ASSIGNEE:

ADVANCED CORNEAL SYSTEMS, INC., (1643981), 15279 Alton Parkway No. 100, Irvine, CA 92618, (US), (Applicant designated States: all)
INVENTOR:
KARAGEOZIAN, Hampar, L., 31021 Marbella Vista, San Juan Capistrano, CA 92675, (US)
KARAGEOZIAN, Vicken, H., 31021 Marbella Vista, San Juan Capistrano, CA 92675, (US)
KENNEY, Maria, Cristina, 18128 Wakecrest Drive, Malibu, CA 90265, (US)
FLORES, Jose Luis Gutierrez, Avenida Emiliano Zapata 19208, Colonia Leyva Aleman, 22500, (MX)
ARAGON, Gabriel Arturo Carpio, Avenida Amado Paniagua 200-302, Colonia Aviacion, 22420, (MX)
NESBURN, Anthony, B., 18128 Wakecrest Drive, Malibu, CA 90265, (US)
LEGAL REPRESENTATIVE:
Meissner, Bolte & Partner (100193), Anwaltssozietat GbR Postfach 86 06 24 , 81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 983084 A1 000308 (Basic)
WO 9852602 981126
APPLICATION (CC, No, Date): EP 98924866 980522; WO 98US10578 980522
PRIORITY (CC, No, Date): US 862620 970522
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/47
NOTE: No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

10/3,AB/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00806570
COMPOSITIONS AND METHODS FOR THE INDUCTION AND TREATMENT OF RETINAL DETACHMENTS
COMPOSITIONS ET PROCEDES PERMETTANT D'INDUIRE ET DE TRAITER LES DECOLLEMENTS DE LA RETINE
Patent Applicant/Assignee:
ISTA PHARMACEUTICALS INC, Suite 100, 15279 Alton Parkway, Irvine, CA 92618, US, US (Residence), US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
KARAGEOZIAN Hampar, 31021 Marbella Vista, San Juan Capistrano, CA 92675, US, US (Residence), US (Nationality), (Designated only for: US)
Legal Representative:
HUNT Dale C (agent), Knobbe, Martens, Olson & Bear, LLP, 16th floor, 620 Newport Center Drive, Newport Beach, CA 92660, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200139765 A2-A3 20010607 (WO 0139765)
Application: WO 2000US42455 20001201 (PCT/WO US0042455)
Priority Application: US 99168830 19991203
Designated States: AE AG AL AM AT (utility model) AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ (utility model) DE (utility model) DK (utility model) DM DZ EE (utility model) ES FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK (utility model) SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 9830
English Abstract
A method comprising administering by ocular route a dose of a glycol ether effective to induce retinal detachment.

10/3,AB/4 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00509581
USE OF HYALURONIDASE TO REDUCE VISCOELASTIC RELATED INCREASES IN INTRAOCULAR PRESSURE
UTILISATION DE HYALURONIDASE AFIN DE DIMINUER LES HAUSSES DE PRESSION INTRAOCULAIRE ASSOCIEES A LA VISCOELASTICITE
Patent Applicant/Assignee:
THE SCHEPENS EYE RESEARCH INSTITUTE INC,
REFOJO Miguel F,
HAROONI Mark,
FREILICH Jonathan M,
ABELSON Mark B,
Inventor(s):
REFOJO Miguel F,
HAROONI Mark,
FREILICH Jonathan M,
ABELSON Mark B,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9940933 A1 19990819
Application: WO 99US3125 19990212 (PCT/WO US9903125)
Priority Application: US 9874837 19980217
Designated States: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 3178
English Abstract
Small doses, less than 15 IU and preferably less than 10 IU per treated eye, of hyaluronidase can safely and effectively be employed to reduce postoperative intraocular pressure caused by residual amounts of hyaluronan used during anterior segment surgical procedures. The hyaluronidase may be administered after surgery, or at 5 IU or less per treated eye concomitantly. Hyaluronidase treatment may be combined with treatments with other medications.

File 348:EUROPEAN PATENTS 1978-2002/Sep W03
File 349:PCT FULLTEXT 1983-2002/UB=20020912,UT=20020905

Set	Items	Description
S1	0	E2
S2	561	VITREOUS()(HUMOR OR HUMOUR)
S3	1625	HYALURONIDASE
S4	13	STREPTOMYCES()HYALUROLYTICUS
S5	30682	PROTEASE
S6	950	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	11	S2(S)S3
S8	0	S7(S)S4:S6
S9	**6**	**S7 AND S4:S6**

S10 5 S7 NOT S9

9/6/1 (Item 1 from file: 440)
13367648 References: 50
Plasmodium falciparum cytoadherence to human placenta: Evaluation of hyaluronic acid and chondroitin 4-sulfate for binding of infected erythrocytes
2001
GENUINE ARTICLE#: 506UL

11/6/1 (Item 1 from file: 440)
09796608 References: 33
TITLE: HYAL2, a human gene expressed in many cells, encodes a lysosomal hyaluronidase with a novel type of specificity
1998
GENUINE ARTICLE#: 114NY

11/6/2 (Item 2 from file: 440)
09485402 References: 12
Screening of pharmaceuticals and drugs in synovial fluid of the knee joint and in vitreous humor by fluorescence polarization immunoassay (FPIA)
1998
GENUINE ARTICLE#: ZN879

11/6/3 (Item 3 from file: 440)
05682284 References: 21
QUANTITATIVE ANALYSIS OF HYALURONAN IN VITREOUS HUMOR USING CAPILLARY ELECTROPHORESIS
1994
GENUINE ARTICLE#: PC634

11/6/4 (Item 4 from file: 440)
04661762 References: 14
TITLE: OPTIMIZATION OF THE USP ASSAY FOR HYALURONIDASE
1993
GENUINE ARTICLE#: LJ294

File 440:Current Contents Search(R) 1990-2002/Sep 27
File 305:Analytical Abstracts 1980-2002/Sep W3
File 50:CAB Abstracts 1972-2002/Aug
File 71:ELSEVIER BIOBASE 1994-2002/Sep W4
File 76:Life Sciences Collection 1982-2002/Sep
File 162:CAB Health 1983-2002/Aug

Set	Items	Description
S1	0	E2
S2	1239	VITREOUS()(HUMOR OR HUMOUR)
S3	3808	HYALURONIDASE
S4	11	STREPTOMYCES()HYALUROLYTICUS
S5	95481	PROTEASE
S6	612	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	12	S2 AND S3
S8	4	S7 AND S4:S6
S9	**1**	**RD (unique items)**
S10	8	S7 NOT S8
S11	**5**	**RD (unique items)**

10/6/1 (Item 1 from file: 370)
00504539 (USE 9 FOR FULLTEXT)
Hyaluronan Synthase of Chlorella Virus PBCV-1
Publication Date: 12-05-1997 (971205)
Word Count: 2049

8/3,AB/2 (Item 1 from file: 128)
DIALOG(R)File 128:PHARMAPROJECTS
(c) 2002 PJB Publications,Ltd. All rts. reserv.
0007811
DRUG NAME: hyaluronidase, Biopharm
ORIGINATOR: Biopharm (UK) [No Development Reported]
SYNONYMS: endo-beta-glucuronidase, Biophar
Orgelase
CHEM NAME: Hyaluronidase (CAS)
CAS REG NO: 9001-54-1
TEXT: Hyaluronidase is a potent and selective enzyme which degrades hyaluronic acid, which was under development by Biopharm in the UK under special licence (Company communication, Sep 1993).
Preclinical
Patents were pending in the US, Europe and Japan. The enzyme had potential uses in cardiovascular medicine, dentistry and ophthalmology. It could have been used as an adjunct for injections of local anaesthetics, since it aids dispersal of the anaesthetic giving a more rapid and further-reaching effect. It had a potential role in the treatment of myocardial infarction and related disorders as it is not inhibited by heparin (Thromb Res, 1989, 55, 791). It may have also been of value in the treatment of disorders of the vitreous humour in the eye, such as vitreous clots and central vein occlusion. Unlike bovine hyaluronidase , it has no effect on chondroitin or any other polysaccharide. It is being developed as a diagnostic for the routine screening of hyaluronic acid in body fluids.
THER. CLASS: C9Z (Cardiovascular)
S1Z (Ophthalmological)
V4Z (Diagnostic)
PHARM. CODE: HYALUR-AG, Enzyme, Hydrolase, Hyaluronidase stimulant, Hyaluronoglucosaminidase stimulant , Mucinase stimulant , E-HY-HYALU-AG, 3.2.1.35
Therapy Pharmacology Status
Reported
LATEST UPD: 19970502 (UN) No development reported
UPDATED: 19970502 (Est) No Development Reported
REVISED: 19970502; 1997

11/3,AB/1 (Item 1 from file: 107)
DIALOG(R)File 107:Adis R&D Insight
(c) 2002 Adis International Ltd. All rts. reserv.
00174024 009346
DRUG NAME: Hyaluronidase (Vitrase) - Ista
RECORD REVISION DATE: 20020122
SYNONYMS: Hyaluronidase - Ista; Vitrase
WHO ATC CODE: A10X - Other Drugs Used in Diabetes; S01K-X - Other Surgical Aids; S01X - Other Ophthalmologicals
EPHMRA ATC CODE: A10X - Other Drugs Used in Diabetes; S1S9 - Other Surgical Aids

MECHANISM OF ACTION: Hyaluronidase stimulants; Enzyme stimulants
ORIGINATOR COMPANY: Ista Pharmaceuticals (USA)
PARENT COMPANY: Ista Pharmaceuticals
LICENSEE: Allergan; Otsuka Pharmaceutical; Sophia Laboratories
OTHER COMPANY: Visionex
HIGHEST PHASE: Registered
DEVELOPMENT STATUS: Registered, Mexico, Vitreous haemorrhage
Phase III, Australia, Vitreous haemorrhage
Phase III, Brazil, Vitreous haemorrhage
Phase III, Canada, Vitreous haemorrhage
Phase III, Europe, Vitreous haemorrhage
Phase III, South Africa, Vitreous haemorrhage
Phase III, USA, Vitreous haemorrhage
Phase II, Mexico, Diabetic retinopathy
Phase II, Singapore, Vitreous haemorrhage

TEXT

Introduction:

Ista Pharmaceuticals (formerly Advanced Corneal Systems) has developed an ophthalmic injectable formulation of hyaluronidase for use in the treatment of vitreous haemorrhage. The enzyme preparation (Vitrase sup(TM)) is injected into the eye causing the vitreous to liquify and the blood to clear so the underlying cause can be identified. Vitrase sup(TM) is being investigated in 2 multinational, placebo controlled, double-blind, randomised trials in patients with severe vitreous haemorrhage. One is being conducted in the US, Mexico and Canada. The second trial is being conducted in Europe, Brazil, Australia and South Africa. Enrolment in both trials has been completed

The first regulatory submission for marketing approval for Vitrase sup(TM) for vitreous haemorrhage was filed in Mexico in June 1998 and it was approved in November 1998 by the Mexican National Ministry of Health. Sophia Laboratories distribute Vitrase sup(TM) in Mexico.

The FDA designated Vitrase sup(TM) a fast track product in October 1998, which means the FDA will facilitate the development and expedite the review of the product. In January 2002, Ista Pharmaceuticals submitted the first section of a New Drug Appliction (NDA) to the US FDA. The sections submitted were the non-clinical pharmacology and toxicology sections. Ista Pharmaceuticals expect to submit the clinical, chemistry and manufacturing and controls sections of the NDA before the end of the third quarter 2002. The final section, which covers manufacturing validation, is expected to be submitted in the first quarter of 2003.

The data from 2 phase III trials was to be unmasked at the end of January 2002, but the company chose not to look at it until a method of analysis for the data has been agreed upon with the FDA. Ista also wanted to come to an agreement with the FDA about future post-approval studies before the phase III data was unmasked, so as to prevent any bias in the future studies. In March 2002, Ista began unmasking the data, revealing that although preliminary efficacy results did not show any statistically significant improvement in the primary endpoint, clinically relevant improvements in visual acuity were observed in patients treated with Vitrase(TM).

A phase II trial in Singapore was being conducted by Visionex. However, in March 2000, Ista completed the acquisition of Visionex.

A pilot phase IIa trial of Vitrase sup(TM) in 60 patients with nonproliferative diabetic retinopathy in Mexico City has been completed. Interim results of the study demonstrated encouraging trends for slowing progression of diabetic retinopathy. In the study, Vitrase sup(TM) was

injected into the vitreous humor causing this to liquify and separate from the retina. It was suggested that it may prevent the growth of abnormal blood vessels in the back of the eye.
In March 2000, subsidiaries of Allergan obtained marketing, sales and distribution agreements from Ista for Vitrase sup(TM) worldwide, except Mexico (until 2004) and Japan. In December 2001, Otsuka gained exclusive rights to develop and commercialise Vitrase sup(TM) in Japan. In July 2002, Ista announced that it has entered into an agreement with Cardinal Health for the manufacture of commercial quantities of Vitrase sup(TM). The agreement covers the US, Canada, Japan and the EU. Cardinal Health will also provide manufacturing- related information for the US NDA.
Ista is also developing hyaluronidase products for the treatment of cataracts (Keratase sup(TM)) and keratoconus (Keraform sup(TM)) (see separate profiles).
ADIS EVALUATION:
Vitreous haemorrhage 60 (Ophthalmic).
PHARMACOLOGY OVERVIEW:
Pharmacodynamics:
Mechanism of action:
Hyaluronidase stimulants
Enzyme stimulants
CLINICAL OVERVIEW:
Route(s) of Administration: Ophthalmic
Drug Interactions:
Unknown.
DRUG NAME: Hyaluronidase (Vitrase) - Ista
SYNONYMS: Hyaluronidase - Ista; Vitrase
MECHANISM OF ACTION: Hyaluronidase stimulants; Enzyme stimulants

11/3,AB,K/2 (Item 1 from file: 129)
DIALOG(R)File 129:PHIND(Archival)

00041692
Biopharm's HLA enzyme product
Scrip 987 p12, April 03, 1985 (19850403)
WORD COUNT: 220
...in wisdom teeth extraction. Another application for Orgelase is in the treatment of disorders of vitreous humour in the eye (90% of which consists of hyaluronic acid), such as vitreous clots and...
...Orgelase is highly specific and potent in its activity against hyaluronic acid, and unlike bovine hyaluronidase, has no effect on chondroitin and its derivatives, or any other polysaccharide. The company suggests...

11/3,AB,K/3 (Item 1 from file: 229)
DIALOG(R)File 229:Drug Info. Fulltext

00999236 AHFS NO: 52.08 AHFS CLASS: Anti-inflammatory Agents
SUBFILE: AHFS Drug Information
MONOGRAPH TITLE: Ketorolac Tromethamine
GENERIC NAME: Ketorolac Tromethamine; Ketorolac
CHEMICAL NAME: 74103-07-4; 74103-06-3
SYNONYMS: Nonsteroidal Anti-inflammatory Agents; NSAIAs, EENT; NSAIDs, EENT; RS 37619
INVESTIGATIONAL NO: RS 37619
BRAND NAME/MANUFACTURER: Acular/Allergan; Acular PF/Allergan
CAS REGISTRY NO: 74103-07-4; 74103-06-3

Subsections: [3224]_Conjunctivitis; [3214]_Postoperative and Posttraumatic Ocular Inflammation; [3214]_Cystoid Macular Edema; [3214]_Inhibition of Intraoperative Miosis; [3224]_Postoperative Ocular Pain and Photophobia; [3574]_Administration; [3524]_Dosage; [3506]_Conjunctivitis; [3506]_Postoperative and Posttraumatic Ocular Inflammation; [3506]_Postoperative Ocular Pain and Photophobia; [3604]_Ocular Effects; [3604]_Systemic Effects; [3644]_Precautions and Contraindications; [3644]_Pediatric Precautions; [3664]_Mutagenicity and Carcinogenicity; [3654]_Pregnancy, Fertility, and Lactation; [3774]_Corticosteroids; [3204]_Ocular Effects; [3204]_Systemic Effects; [3814]_Absorption; [3824]_Distribution; [3834]_Elimination; [3104]_Chemistry; [3304]_Stability; [3404]_Ketorolac Tromethamine
PHARMACOKINETICS (PK):
...g., sclera), intraocular tissues (e.g., aqueous humor, choroid-retina, iris, ciliary body), lens, and vitreous humor ;(14,16,78) concentrations are highest in scleral and corneal tissues and lowest in the...
DRUG INTERACTIONS (DI):
... has been used in conjunction with injectable sedatives (e.g., diazepam, hydroxyzine, lorazepam, promethazine hydrochloride), hyaluronidase , and/or local anesthetics (bupivacaine hydrochloride, lidocaine hydrochloride, tetracaine hydrochloride).(17,19,85)
Corticosteroids
[3775...

File 370:Science 1996-1999/Jul W3
File 107:Adis R&D Insight 1986-2002/Sep W4
File 128:PHARMAPROJECTS 1980-2002/Sep W4
File 129:PHIND(Archival) 1980-2002/Sep W4
File 229:Drug Info. Fulltext 2002
File 484:Periodical Abs Plustext 1986-2002/Sep W4

Set	Items	Description
S1	0	E2
S2	91	VITREOUS()(HUMOR OR HUMOUR)
S3	130	HYALURONIDASE
S4	2	STREPTOMYCES()HYALUROLYTICUS
S5	6122	PROTEASE
S6	436	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	0	S1(S)S2
S8	**2**	**S2(S)S3**
S9	6	S2 AND S3
S10	**2**	**S9 AND S4:S6**
S11	**3**	**S9 NOT (S8 OR S10)**

7/9/1 (Item 1 from file: 763)
DIALOG(R)File 763:Freedonia Market Res.
(c) 2002 Freedonia Group Inc. All rts. reserv.
00219311
PRIVATE & START-UP COMPANY PROFILES: Ista Pharmaceuticals
Main Title: BIOTECHNOLOGY PHARMACEUTICALS - PRIVATE COMPANIES REPORT
Pub. Date: DECEMBER 2000
Source: THE FREEDONIA GROUP, INC.
Telephone: (440) 684-9600
Word Count: 517 (1 pp.)
Language: English
Ista Pharmaceuticals Incorporated

15279 Alton Parkway, Building 100
Irvine, CA 92618
County: Orange
County Code: 06059
Phone: 949-788-6000
Fax: 949-788-6010
Annual Sales: not applicable, development stage company
Employment: 35 (verified by company, 10/00)
Principal Owner(s): Publicly Traded
Key Executive: Edward H. Danse, President and CEO
Key Products: development of hyaluronidase enzyme-based treatments for eye diseases and conditions
Census Code SIC(s): 8731
SIC Description(s): commercial physical and biological research

Ista Pharmaceuticals, formerly known as Advanced Corneal Systems Incorporated, is a developmental stage company which discovers hyaluronidase enzyme-based treatments for eye diseases and conditions. The Company, formed in 1992, completed its initial public offering of three million shares of common stock at $10.50 per share in August 2000, with gross proceeds from the offering totaling approximately $32 million. Ista began trading on the NASDAQ stock exchange under the symbol ISTA. In March 2000, the Company acquired Visionx Party Limited (Singapore), a firm involved in the development and commercialization of therapeutic ophthalmic drugs and non-surgical vision correction systems. Ista maintains a 13,000-square-foot headquarters and laboratory facility in Irvine, California.

The Company's developmental drug candidates include VITRASE, KERATASE and KERAFORM hyaluronidase products. Hyaluronidase is a group of enzymes which can digest proteoglycan carbohydrate molecules, including hyaluron, hyaluronic acid and chondroitin sulphate. In the eye, the enzymes can be used to treat such diseases as vitreous hemorrhage and diabetic retinopathy. VITRASE is in Phase III clinical trials for the treatment of severe vitreous hemorrhage, which is caused by the rupturing of retinal blood vessels which bleed into the vitreous humor, or clear gel-like substance that fills the back of the eye. This product is also undergoing Phase IIa clinical trials in Mexico for the treatment of diabetic retinopathy, a progressive disease which causes abnormal changes in the blood vessels of the eye resulting in blindness. In March 2000, Ista established an agreement with Allergan for the marketing and distribution of VITRASE. Under the terms of the agreement, Ista is responsible for all product development, clinical trials, regulatory approvals and manufacturing of VITRASE, while Allergan will handle the marketing, sale and distribution of the product in the US and worldwide, excluding Mexico and Japan. Profits from the sale of VITRASE in the US will be split evenly between the two companies. The agreement also includes milestone payments of up to $35 million to Ista from Allergan.

KERATASE is in Phase IIb clinical trials for the treatment of corneal opacification, a condition which occurs when the cornea becomes scarred, cloudy or opaque. The product is a more concentrated formulation of hyaluronidase than VITRASE. KERAFORM is a proprietary system for the treatment of keratocunus, a progressive thinning of the cornea. The KERAFORM system is designed to reshape the cornea in order to stabilize, improve or correct keratocunus.

Ista maintains agreements with Biozyme and Prima Pharma for the supply of its hyaluronidase products. Biozyme supplies current Good

Manufacturing Practices-grade hyaluronidase which has been lyophilized. The raw material is delivered to Prima Pharm, Ista's contract manufacturer for the formulation and filling of the final hyaluronidase products.
THIS IS THE FULL-TEXT.
Copyright THE FREEDONIA GROUP, INC. 2000
Country: UNITED STATES
Industry: BIOTECHNOLOGY, PHARMACEUTICALS
Company Names (DIALOG Generated): Allergan ; Annual Sales ; Key Products ; Visionx Party Limited

7/9/2 (Item 1 from file: 767)
DIALOG(R)File 767:Frost & Sullivan Market Eng
(c) 2002 Frost & Sullivan Inc. All rts. reserv.
00981184
U.S. DIABETIC RETINOPATHY PHARMACEUTICALS MARKET: Market and Technology Trends: Research Directions: Other Treatments; Hyaluronidase Enzyme for Depolarizing Hyaluronic Acid
Main Title: U.S. LEADING OPHTHALMIC DISEASES MARKETS
Pub. Date: May 2002
Source: Frost & Sullivan
Telephone: US (415) 961 - 1000; London 071 730 3438
Word Count: 248 (1 pp.)
Language: English
Other Treatments
Control Delivery Systems along with Bausch and Lomb have developed a tiny implantable device called the Envision TD, designed to treat problems at the back of the eye. The implant is surgically placed inside the eye and gradually releases fluocinolone (an anti-inflammatory) over a long period of time. This technology has already been used to treat CMV related to AIDS. The Envision TD implant is currently being studied for the treatment of DME and is in Phase III clinical trials. Trials have shown that patients administered 5-6 mcg/day of fluocinolone had a rapid resolution of edema and an improvement in visual acuity.
Hyaluronidase Enzyme for Depolarizing Hyaluronic Acid
ISTA Pharmaceutical's Vitrase has recently completed a Phase IIb pilot study in Mexico for the treatment of DR. At the annual meeting of the American Academy of Ophthalmology in October 2000, interim data from the Phase IIa pilot study was presented that demonstrated Vitrase safely induced a posterior vitreous detachment (PVD) in 60 percent of the eyes treated with a single dose of Vitrase. PVD is the separation of the vitreous humor from the retina, which is believed to slow or stop the progression of DR.
THIS IS THE FULL-TEXT.
Copyright Frost & Sullivan 2002
Country: UNITED STATES
Industry: PHARMACEUTICALS
Company Names (DIALOG Generated): American Academy of Ophthalmology ; Bausch and Lomb ; Control Delivery Systems ; ISTA Pharmaceutical

File 763:Freedonia Market Res. 1990-2002/Sep
File 767:Frost & Sullivan Market Eng 2002/Aug

Set	Items	Description
S1	0	E2
S2	4	VITREOUS()(HUMOR OR HUMOUR)

S3	11	HYALURONIDASE
S4	0	STREPTOMYCES()HYALUROLYTICUS
S5	671	PROTEASE
S6	253	TURBIDITY()REDUC???()(UNIT OR UNITS) OR TRU
S7	**2**	**S2 AND S3**

L7 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:582655 HCAPLUS
DN 129:287201
TI HYAL2, a human gene expressed in many cells, encodes a lysosomal hyaluronidase with a novel type of specificity

L7 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:536958 HCAPLUS
DN 127:158783
TI Methods for detection and evaluation of bladder cancer

L7 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:533954 HCAPLUS
DN 119:133954
TI Optimization of the USP assay for hyaluronidase

L7 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:250843 HCAPLUS
DN 118:250843
TI Hyaluronidase degradation of hyaluronic acid from different sources: Influence of the hydrolysis conditions on the production and the relative proportions of tetra- and hexasaccharide produced

L7 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:469699 HCAPLUS
DN 109:69699
TI Quantitation of hyaluronic acid in tissues by ion-pair reverse-phase high-performance liquid chromatography of oligosaccharide cleavage products

L7 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:550546 HCAPLUS
DN 107:150546
TI Analysis of vitreous and aqueous levels of hyaluronic acid: application of high-performance liquid chromatography

L7 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:21826 HCAPLUS
DN 102:21826
TI Degradation of glycosaminoglycans by extracts of calf vitreous hyalocytes

L7 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1975:122699 HCAPLUS
DN 82:122699
TI Experimental depolymerization of hyaluronic acid of rabbit vitreous. III. Immunological investigations

L7 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1972:136429 HCAPLUS
DN 76:136429
TI Inhibitory activity of heparin on the action of hyaluronidase on rabbit and dog vitreous

L7 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:416761 HCAPLUS
DOCUMENT NUMBER: 135:24701

TITLE: **Compositions and methods for the induction and treatment of retinal detachments**
INVENTOR(S): Karageozian, Hampar
PATENT ASSIGNEE(S): Ista Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039765	A2	20010607	WO 2000-US42455	20001201
WO 2001039765	A3	20020510		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-168830P P 19991203

AB A method comprising administering by ocular route a dose of a glycol ether effective to induce retinal detachment is disclosed.

(FILE 'HOME' ENTERED AT 15:00:21 ON 27 SEP 2002)
FILE 'REGISTRY' ENTERED AT 15:00:29 ON 27 SEP 2002
E HYALURONIDASE/CN
L1 4 S E3
FILE 'HCAPLUS' ENTERED AT 15:00:41 ON 27 SEP 2002
L2 1617 S VITREOUS HUMOR OR VITREOUS HUMOUR
L3 29 S STREPTOMYCES HYALUROLYTICUS
L4 71562 S PROTEASE
L5 935 S TURBIDITY REDUCING UNIT? OR TURBIDITY REDUCTION UNIT? OR TRU
L6 2354 S L1
L7 12 S L2 AND L6
L8 0 S L7 AND (L3 OR L4 OR L5)

Searched for all of the words: "**turbidity reducing unit**".
Found: **5 total | 4 journal results | 1 Web results**
Sort by relevance | Sort by date

1. H7981-10 Hyaluronidase, Streptomyces hyalurolyticus Molecular Biology Grade
Apr 2002
...ferricyanide Unit Definition: One TRU (**Turbidity Reducing Unit**) is the amount of enzyme which causes...ferricyanide Unit Definition: One TRU (**Turbidity Reducing Unit**) is the amount of enzyme which causes...
[http://www.usbio.net/bin/product.pl?product=2800]
similar results

Searched for all of the words: "**turbidity reducing unit**".
Found: **5 total | 4 journal results | 1 Web results**
Sort by relevance | Sort by date

☐ **1.** Purification and microsequencing of hyaluronidase isozymes from human urine
Csoka, T.B. / Frost, G.I. / Wong, T. / Stern, R., *FEBS Letters*, Nov 1997
We recently cloned the major hyaluronidase of human plasma, which we termed HYAL1. All hyaluronidase activity could be purified from human urine on an anti-HYAL1 monoclonal antibody column. However, urine contains two hyaluronidases of...
Full text article available from SCIENCE DIRECT
similar results

☐ **2.** Effect of in vitro aging on the biosynthesis of glycosaminoglycans by human skin fibr...
Fodil-Bourahla, I. / Drubaix, I. / Robert, L., *Mechanisms of Ageing and Development*, Jan 1999
The incorporation of a radioactive precursor ^{3}H-glucosamine in glycoconjugates, essentially glycosaminoglycans (GAG) was evaluated in the culture medium and cell fraction of human skin fibroblasts. Using increasing passage numbers, we...
Full text article available from SCIENCE DIRECT
similar results

☐ **3.** Stimulation of hyaluronan synthesis by tumor necrosis factor-? is mediated by the p5...
Ohkawa, T. / Ueki, N. / Taguchi, T. / Shindo, Y. / Adachi, M. / Amuro, Y. / Hada, T. / Higashino, K., *Biochimica et Biophysica Acta (BBA)/Molecular Cell*

Biochimica et Biophysica Acta (BBA)/Molecular Cell Research, Jan 1999
The lesions of fibrocontractive diseases result from an excessive myofibroproliferative response to numerous forms of inflammatory stimuli, which elicit the net deposition of extracellular matrix (ECM) in the interstitium of the affected...
Full text article available fr m SCIENCE DIRECT
similar results

refine

☐ **4.** Inhibition of hyaluronan synthesis by vesnarinone in cultured human myofibroblasts
Ueki, N. / Taguchi, T. / Takahashi, M. / Adachi, M. / Ohkawa, T. / Amuro, Y. / Hada, T. / Higashino, K., *Biochimica et Biophysica Acta (BBA)/Molecular Cell Research*, Feb 2000
Hyaluronan (HA), which is a major component of the extracellular matrix (ECM), is regulated during myofibroproliferative responses to numerous forms of inflammatory stimuli. It is a key factor involved in cellular migration and...
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tunica [BIOL] A membrane or layer of tissue that covers or envelops an organ or other anatomical structure. { 'tü·nə·kə }

tunica adventitia *See* adventitia. { 'tü·nə·kə ˌad·vən'tish·ə }

tunica intima *See* intima. { 'tü·nə·kə 'in·tə·mə }

tunica mucosa *See* mucous membrane. { 'tü·nə·kə myü'kō·zə }

Tunicata [INV ZOO] A subphylum of the Chordata characterized by restriction of the notochord to the tail and posterior body of the larva, absence of mesodermal segmentation, and secretion of an outer covering or tunic about the body. { ˌtü·nə'käd·ə }

tuning [COMPUT SCI] The use of various techniques involving adjustments to both hardware and software to improve the operating efficiency of a computer system. [ELECTR] The process of adjusting the inductance or the capacitance or both in a tuned circuit, for example, in a radio, television, or radar receiver or transmitter, so as to obtain optimum performance at a selected frequency. { 'tün·iŋ }

tuning capacitor [ELEC] A variable capacitor used for tuning purposes. { 'tün·iŋ kə,pas·əd·ər }

tuning circuit *See* tuned circuit. { 'tün·iŋ ˌsər·kət }

tuning coil [ELEC] A variable inductance coil for adjusting the frequency of an oscillator or tuned circuit. { 'tün·iŋ ˌkȯil }

tuning core [ELECTROMAG] A ferrite core that is designed to be moved in and out of a coil or transformer to vary the inductance. { 'tün·iŋ ˌkȯr }

tuning fork [ENG] A U-shaped bar for hard steel, fused quartz, or other elastic material that vibrates at a definite natural frequency when struck or when set in motion by electromagnetic means; used as a frequency standard. { 'tün·iŋ ˌfȯrk }

tuning indicator [ELECTR] A device that indicates when a radio receiver is tuned accurately to a radio station, such as a meter or a cathode-ray tuning indicator; it is connected to a circuit having a direct-current voltage that varies with the strength of the incoming carrier signal. { 'tün·iŋ ˌin·də,kād·ər }

tuning range [ELECTR] The frequency range over which a receiver or other piece of equipment can be adjusted by means of a tuning control. { 'tün·iŋ ˌrānj }

tuning screw [ELECTROMAG] A screw that is inserted into the top or bottom wall of a waveguide and adjusted as to depth of penetration inside for tuning or impedance-matching purposes. { 'tün·iŋ ˌskrü }

tuning stub [ELECTROMAG] Short length of transmission line, usually shorted at its free end, connected to a transmission line for impedance-matching purposes. { 'tün·iŋ ˌstəb }

tuning susceptance [ELECTR] Normalized susceptance of an anti-transmit-receive tube in its mount due to the deviation of its resonant frequency from the desired resonant frequency. { 'tün·iŋ sə,sep·təns }

turning value [MATH] A relative maximum or relative minimum of a function. { 'tərn·iŋ ˌvalv }

tuning wand [ELEC] Rod of insulating material having a brass plug at one end and a powered iron core at the other end; used for checking receiver alignment. { 'tün·iŋ ˌwänd }

tunnel [ENG] A long, narrow, horizontal or nearly horizontal underground passage that is open to the atmosphere at both ends; used for aqueducts and sewers, carrying railroad and vehicular traffic, various underground installations, and mining. { 'tən·əl }

tunnel-bearing grease [MATER] Lubricating grease for the main engine and propeller shaft (in the shaft tunnel) of ships. { 'tən·əl ˌber·iŋ ˌgrēs }

tunnel blasting [ENG] A method of heavy blasting in which a heading is driven into the rock and afterward filled with explosives in large quantities, similar to a borehole, on a large scale, except that the heading is usually divided in two parts on the same level at right angles to the first heading, forming in plan a T, the ends of which are filled with explosives and the intermediate parts filled with inert material like an ordinary borehole. { 'tən·əl ˌblast·iŋ }

tunnel borer [MECH ENG] Any boring machine for making a tunnel; often a ram armed with cutting faces operated by compressed air. { 'tən·əl ˌbȯr·ər }

tunnel carriage [MECH ENG] A machine used for rapid tunneling, consisting of a combined drill carriage and manifold for water and air so that immediately the carriage is at the face, drilling may commence with no lost time for connecting up or waiting for drill steels; the air is supplied at pressures of 95 to 100 pounds per square inch (655,000 to 689,000 pascals). { 'tən·əl ˌkar·ij }

tunnel cave *See* natural tunnel. { 'tən·əl ˌkāv }

tunnel diode [ELECTR] A heavily doped junction diode that has a negative resistance at very low voltage in the forward bias direction, due to quantum-mechanical tunneling, and a short circuit in the negative bias direction. Also known as Esaki tunnel diode. { 'tən·əl ˌdī,ōd }

tunnel effect [QUANT MECH] The ability of a particle to pass through a region of finite extent in which the particle's potential energy is greater than its total energy; this is a quantum-mechanical phenomenon which would be impossible according to classical mechanics. { 'tən·əl i,fekt }

tunnel gun [ORD] A gun mounted inside an airplane fuselage and firing through an aperture. { 'tən·əl ˌgən }

tunneling cryotron [ELECTR] A low-temperature current-controlled switching device that has two electrodes of superconducting material separated by an insulating film, forming a Josephson junction, and a control line whose currents generate magnetic fields that switch the device between two states characterized by the presence or absence of electrical resistance. { 'tən·əl·iŋ 'krī·ə,trän }

tunneling microscope *See* scanning tunneling microscope. { 'tən·əl·iŋ 'mī·krə,skōp }

tunnel junction [ELECTR] A two-terminal electronic device having an extremely thin potential barrier to electron flow, so that the transport characteristic (the current-voltage curve) is primarily governed by the quantum-mechanical tunneling process which permits electrons to penetrate the barrier. { 'tən·əl ˌjəŋk·shən }

tunnel liner [CIV ENG] Any of various materials, especially timber, concrete, and cast iron, applied to the inner surface of a vehicular or railroad tunnel. [MIN ENG] The timber, brick, concrete, or steel supports erected in a mine tunnel to maintain dimensions and safe working conditions. { 'tən·əl ˌlīn·ər }

tunnel rectifier [ELECTR] Tunnel diode having a relatively low peak-current rating as compared with other tunnel diodes used in memory-circuit applications. { 'tən·əl ˌrek·tə,fī·ər }

tunnel resistor [ELECTR] Resistor in which a thin layer of metal is plated across a tunneling junction, to give the combined characteristics of a tunnel diode and an ordinary resistor. { 'tən·əl ri,zis·tər }

tunnel set [MIN ENG] Timbers 6 to 8 inches (15 to 20 centimeters) in diameter and of sufficient height to support the roof of the tunnel. { 'tən·əl ˌset }

tunnel system [MIN ENG] A method of mining in which tunnels or drifts are extended at regular intervals from the floor of the pit into the ore body. { 'tən·əl ˌsis·təm }

tunnel triode [ELECTR] Transistorlike device in which the emitter-base junction is a tunnel diode and the collector-base junction is a conventional diode. { 'tən·əl ˌtrī,ōd }

tunnel vault *See* barrel vault. { 'tən·əl ˌvȯlt }

Tupaiidae [VERT ZOO] The tree shrews, a family of mammals in the order Insectivora. { tü'pī·ə,dē }

tupelo [BOT] Any of various trees belonging to the genus *Nyssa* of the sour gum family, Nyssaceae, distinguished by small, obovate, shiny leaves, a small blue-black drupaceous fruit, and branches growing at a wide angle from the axis. { 'tü·pə,lō }

tuple [COMPUT SCI] A horizontal row of data items in a relational data structure; corresponds to a record or segment in other types of data structures. { 'tü·pəl }

turanite [MINERAL] $Cu_5(VO_4)_2(OH)_4$ An olive green, orthorhombic mineral consisting of basic copper vanadate; occurs as reniform crusts and spherical concretions. { 'tůr·ə,nīt }

Turbellaria [INV ZOO] A class of the phylum Platyhelminthes having bodies that are elongate and flat to oval or circular in cross section. { ˌtər·bə'lar·ē·ə }

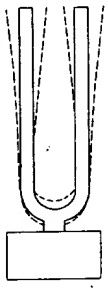
turbidimeter [OPTICS] A device that measures the loss in intensity of a light beam as it passes through a solution with particles large enough to scatter the light. { ˌtər·bə'dim·əd·ər }

turbidimetric analysis [ANALY CHEM] A scattered-light procedure for the determination of the weight concentration of particles in cloudy, dull, or muddy solutions; uses a device that measures the loss in intensity of a light beam as it passes through the solution. Also known as turbidimetry. { ˌtər·bə·də'me·trik ə'nal·ə·səs }

turbidimetric titration [ANALY CHEM] Titration in which the end point is indicated by the developing turbidity of the titrated solution. { ˌtər·bə·də'me·trik tī,trā·shən }

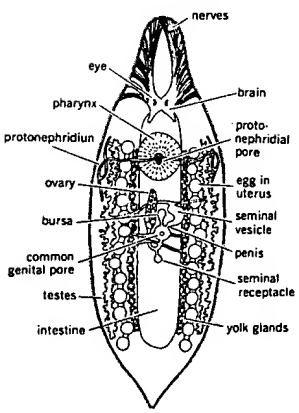
turbidimetry *See* turbidimetric analysis. { ˌtər·bə'dim·ə·trē }

TUNING FORK



A tuning fork vibrating at its fundamental frequency.

TURBELLARIA



A typical hermaphroditic turbellarian, *Mesostoma ehrenbergii wardii*.

turbidite [GEOL] Any sediment or rock transported and deposited by a turbidity current, generally characterized by graded bedding, large amounts of matrix, and commonly exhibiting a Bouma sequence. { 'tər·bə,dīt }

turbidity [ANALY CHEM] **1.** Measure of the clarity of an otherwise clear liquid by using colorimetric scales. **2.** Cloudy or hazy appearance in a naturally clear liquid caused by a suspension of colloidal liquid droplets or fine solids. [ASTRON] The formation of disks centered on stars in long-exposure photographs as a result of light scattering by grains in the emulsion. [METEOROL] Any condition of the atmosphere which reduces its transparency to radiation, especially to visible radiation. { tər'bid·əd·ē }

turbidity coefficient [OPTICS] A factor in the absorption (light) law equation that describes the extinction of the incident light beam. { tər'bid·əd·ē ,kō·i,fish·ənt }

turbidity current [OCEANOGR] A highly turbid, relatively dense current carrying large quantities of clay, silt, and sand in suspension which flows down a submarine slope through less dense sea water. Also known as density current; suspension current. { tər'bid·əd·ē ,kə·rənt }

turbidity factor [GEOPHYS] A measure of the atmospheric transmission of incident solar radiation; if I_0 is the flux density of the solar beam just outside the earth's atmosphere, I the flux density measured at the earth's surface with the sun at a zenith distance which implies an optical air mass m, and $I_{m,w}$ the intensity which would be observed at the earth's surface for a pure atmosphere containing 1 centimeter of precipitable water viewed through the given optical air mass, then turbidity factor θ is given by $\theta = (\ln I_0 - \ln I)/(\ln I_0 - \ln I_{m,w})$. { tər'bid·əd·ē ,fak·tər }

turbidostat [MICROBIO] A device in which a bacterial culture is maintained at a constant volume and cell density (turbidity) by adjusting the flow rate of fresh medium into the growth tube by means of a photocell and appropriate electrical connections. { tər'bid·ə,stat }

turbinate [BOT] Shaped like an inverted cone. [INV ZOO] Spiral with rapidly decreasing whorls from base to apex. { 'tər·bə·nət }

turbine [MECH ENG] A fluid acceleration machine for generating rotary mechanical power from the energy in a stream of fluid. { 'tər·bən }

turbine generator [ELEC] An electric generator driven by a steam, hydraulic, or gas turbine. { 'tər·bən ,jen·ə,rād·ər }

turbine propulsion [MECH ENG] Propulsion of a vehicle or vessel by means of a steam or gas turbine. { 'tər·bən prə,pəl·shən }

turbine pump *See* regenerative pump. { 'tər·bən ,pəmp }

Turbinidae [INV ZOO] A family of gastropod mollusks including species of top shells. { tər'bin·ə,dē }

turbining [MECH ENG] The removal of scale or other foreign material from the internal surface of a metallic cylinder. { 'tər·bən·iŋ }

turboalternator [ELEC] An alternator, such as a synchronous generator, which is driven by a steam turbine. { ,tər·bō'ȯl·tər,nād·ər }

turboblower [MECH ENG] A centrifugal or axial-flow compressor. { 'tər·bō,blō·ər }

turbodrill [PETRO ENG] A rotary tool used in drilling oil or gas wells in which the bit is rotated by a turbine motor inside the well. { 'tər·bō,dril }

turbofan [AERO ENG] An air-breathing jet engine in which additional propulsive thrust is gained by extending a portion of the compressor or turbine blades outside the inner engine case. { 'tər·bō,fan }

turbogrid plate [CHEM ENG] A tray for distillation columns that consists of a flat grid of parallel slots extending over the entire cross-sectional area of the column; the liquid level on each tray is maintained by a dynamic balance between down-flowing liquid and up-flowing vapor. { 'tər·bō,grid 'plāt }

turbojet [AERO ENG] A jet engine incorporating a turbine-driven air compressor to take in and compress the air for the combustion of fuel (or for heating by a nuclear reactor), the gases of combustion (or the heated air) being used both to rotate the turbine and to create a thrust-producing jet. { 'tər·bō,jet }

turbonada [METEOROL] A short thundersquall on the north Spanish coast, sometimes accompanied by waterspouts. { tər·bə'näd·ə }

turboprop [AERO ENG] A gas turbine power plant that produces shaft power to drive aircraft propellers. { 'tər·bō,präp }

turbopump [MECH ENG] A pump that is powered by a turbine. { 'tər·bō,pəmp }

turboramjet [AERO ENG] An aircraft engine that is a hybrid of a turbofan and a ramjet; operates as a ramjet for efficient propulsion at very high supersonic cruise speeds, or as a turbofan for relatively efficient propulsion at low flight speeds. { ,tər·bō'ram,jet }

turboshaft [MECH ENG] A gas turbine engine that is similar to a turboprop but operates through a transmission system to power a device such as a helicopter rotor or pump. { 'tər·bō,shaft }

turbosphere [METEOROL] The region of the atmosphere in which turbulence frequently exists. { 'tər·bə,sfir }

turbosupercharger [MECH ENG] A centrifugal air compressor, gas-turbine driven, usually used to increase induction system pressure in an internal combustion reciprocating engine. { ,tər·bō'sü·pər,chär·jər }

turbulence *See* turbulent flow. { 'tər·byə·ləns }

turbulence energy *See* eddy kinetic energy. { 'tər·byə·ləns ,en·ər·jē }

turbulent boundary layer [FL MECH] The layer in which the Reynolds stresses are much larger than the viscous stresses. { 'tər·byə·lənt 'baün·drē ,lā·ər }

turbulent burner [ENG] An atomizing burner which mixes fuel and air to produce agitated flow. { 'tər·byə·lənt 'bər·nər }

turbulent diffusion *See* eddy diffusion. { 'tər·byə·lənt di'fyü·zhən }

turbulent flow [FL MECH] Motion of fluids in which local velocities and pressures fluctuate irregularly, in a random manner. Also known as turbulence. { 'tər·byə·lənt 'flō }

turbulent flux *See* eddy flux. { 'tər·byə·lənt 'fləks }

turbulent heat conduction [OCEANOGR] Conduction of heat in water by lateral and vertical eddy diffusion, with currents. { 'tər·byə·lənt 'hēt kən,dək·shən }

turbulent Lewis number [PHYS] A dimensionless number used in the study of combined turbulent heat and mass transfer, equal to the ratio of the eddy mass diffusivity to the eddy thermal diffusivity. Symbolized Le_T. { 'tər·byə·lənt 'lü·əs ,nəm·bər }

turbulent Prandtl number [PHYS] A dimensionless number used in the study of heat transfer in turbulent flow, equal to the ratio of the eddy viscosity to the eddy thermal diffusivity. Symbolized Pr_T. { 'tər·byə·lənt 'prənt·əl ,nəm·bər }

turbulent Schmidt number [FL MECH] A dimensionless number used in the study of mass transfer in turbulent flow, equal to the ratio of the eddy viscosity to the eddy mass diffusivity. Symbolized Sc_T. { 'tər·byə·lənt 'shmit ,nəm·bər }

turbulent shear force [FL MECH] A shear force in a fluid which arises from turbulent flow. { 'tər·byə·lənt 'shir ,fȯrs }

turbulization [ENG] In a heat-transfer process involving the interaction of a solid, heat-conducting, and impermeable surface with a surrounding fluid, destruction of the boundary layer in order to intensify the convective heat transfer. { ,tər·bə·lə'zā·shən }

Turdidae [VERT ZOO] The thrushes, a family of passeriform birds in the suborder Oscines. { 'tər·də,dē }

turgid [MED] Swollen and congested. { 'tər·jəd }

turgor [BOT] Distension of a plant cell wall and membrane by the fluid contents. { 'tər·gər }

turgor movement [BOT] A reversible change in the position of plant parts due to a change in turgor pressure in certain specialized cells; movement of *Mimosa* leaves when touched is an example. { 'tər·gər ,müv·mənt }

turgor pressure [BOT] The actual pressure developed by the fluid content of a turgid plant cell. { 'tər·gər ,presh·ər }

Turing computable function [MATH] A function that can be computed on a Turing machine. { 'tür·iŋ kəm'pad·ə·bəl 'fəŋk·shən }

Turing machine [COMPUT SCI] A mathematical idealization of a computing automation similar in some ways to real computing machines; used by mathematicians to define the concept of computability. { 'tür·iŋ mə,shēn }

Turing's thesis *See* Church's thesis. { 'tür·iŋz ,thē·səs }

turion [BOT] A scaly shoot, such as asparagus, developed from an underground bud. { 'tür·ē,ən }

turkey [VERT ZOO] Either of two species of wild birds, and any of various derived domestic breeds, in the family Meleagrididae characterized by a bare head and neck, and in the male

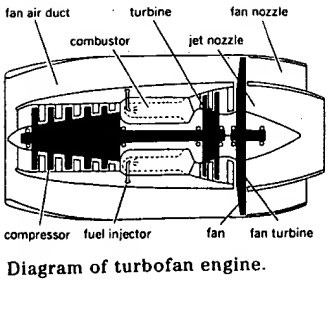


Diagram of turbofan engine.